

Acta Crystallographica Section E

Structure Reports

Online

ISSN 1600-5368

L-Leucylglycylglycine

Masanori Ootaki,^{a*} Yukino Nawa,^a Tomoko Hiroi,^a
Hiroaki Matsui^{a,b} and Yoko Sugawara^c^aInstitute of Radioisotope Research, St. Marianna University Graduate School of Medicine, 2-16-1 Sugao, Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan,^bDepartment of Molecular and Behavioral Neuroscience, St. Marianna University Graduate School of Medicine, 2-16-1 Sugao, Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan, and ^cSchool of Science, Kitasato University, 1-15-1 Kitasato, Minami-ku, Sagami-hara, Kanagawa 252-0373, Japan
Correspondence e-mail: m_ootaki@marianna-u.ac.jp

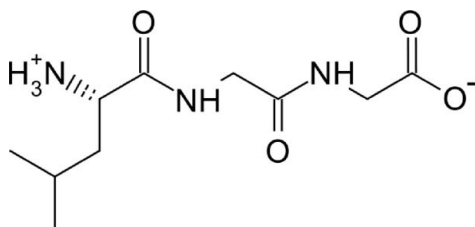
Received 12 March 2013; accepted 27 March 2013

Key indicators: single-crystal X-ray study; $T = 173$ K; mean $\sigma(\text{C}-\text{C}) = 0.003$ Å; R factor = 0.038; wR factor = 0.087; data-to-parameter ratio = 16.4.

In the title compound, $\text{C}_{10}\text{H}_{19}\text{N}_3\text{O}_4$, the N- and C-termini are protonated and ionized, respectively, and the molecule forms a zwitterion. The main chain is in a folded form. In the crystal, the N-terminal $-\text{NH}_3^+$ group hydrogen bonds to three C-terminal $-\text{COO}^-$ groups and one carbonyl O atom, forming a three-dimensional network. In addition, an $\text{N}-\text{H}\cdots\text{O}$ hydrogen bond between the amide groups of the middle glycine residue and a $\text{C}-\text{H}\cdots\text{O}$ interaction continue along the a -axis direction. The side chains of the leucyl residues form a hydrophobic region along the a axis.

Related literature

For related structures of L-leucylglycylglycine, see: Goswami *et al.* (1977); Srikrishnan & Parthasarathy (1987); Kiyotani & Sugawara (2012).



Experimental

Crystal data

 $\text{C}_{10}\text{H}_{19}\text{N}_3\text{O}_4$
 $M_r = 245.28$ Orthorhombic, $P2_12_12_1$
 $a = 5.391$ (5) Å $b = 11.742$ (10) Å
 $c = 19.975$ (16) Å
 $V = 1264.4$ (19) Å³
 $Z = 4$ Mo $K\alpha$ radiation
 $\mu = 0.10$ mm⁻¹
 $T = 173$ K
 $0.48 \times 0.18 \times 0.08$ mm

Data collection

Rigaku Mercury CCD area-detector
diffractometer
9374 measured reflections2887 independent reflections
2200 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.070$

Refinement

 $R[F^2 > 2\sigma(F^2)] = 0.038$
 $wR(F^2) = 0.087$
 $S = 0.96$
2887 reflections
176 parameters
3 restraintsH atoms treated by a mixture of
independent and constrained
refinement
 $\Delta\rho_{\text{max}} = 0.14$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.17$ e Å⁻³

Table 1

Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$\text{N1}-\text{H1}\cdots\text{O3}^{\text{i}}$	0.97 (3)	1.78 (3)	2.743 (2)	168 (2)
$\text{N1}-\text{H2}\cdots\text{O4}^{\text{ii}}$	0.92 (2)	1.94 (2)	2.822 (2)	160 (2)
$\text{N1}-\text{H2}\cdots\text{O3}^{\text{ii}}$	0.92 (2)	2.52 (2)	3.260 (2)	138 (2)
$\text{N1}-\text{H3}\cdots\text{O1}^{\text{iii}}$	0.89 (2)	2.45 (2)	3.031 (2)	123 (2)
$\text{N1}-\text{H3}\cdots\text{O3}^{\text{iv}}$	0.89 (2)	2.05 (2)	2.870 (2)	151 (2)
$\text{N2}-\text{H5}\cdots\text{O2}^{\text{v}}$	0.83 (2)	2.05 (2)	2.832 (2)	155 (2)
$\text{C1}-\text{H4}\cdots\text{O1}^{\text{v}}$	1.00	2.33	3.269 (2)	155

Symmetry codes: (i) $-x + \frac{1}{2}, -y + 1, z - \frac{1}{2}$; (ii) $-x - \frac{1}{2}, -y + 1, z - \frac{1}{2}$; (iii) $x - \frac{1}{2}, -y + \frac{3}{2}, -z + 1$; (iv) $-x, y + \frac{1}{2}, -z + \frac{3}{2}$; (v) $x - 1, y, z$.

Data collection: *CrystalClear* (Rigaku, 2006); cell refinement: *CrystalClear*; data reduction: *CrystalClear*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXL97* (Sheldrick, 2008) and *Yadokari-XG 2009* (Kabuto *et al.*, 2009).

This work was partially supported by the JSPS KAKENHI (grant Nos. 24659548 and 23540478) and MEXT KAKENHI (grant No. 23108003).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: IS5257).

References

- Goswami, K. N., Yadava, V. S. & Padmanabhan, V. M. (1977). *Acta Cryst.* **B33**, 1280–1283.
Kabuto, C., Akine, S., Nemoto, T. & Kwon, E. (2009). *J. Cryst. Soc. Jpn.* **51**, 218–224.
Kiyotani, T. & Sugawara, Y. (2012). *Acta Cryst.* **C68**, o498–o501.
Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.
Rigaku (2006). *CrystalClear*. Rigaku Corporation, Tokyo, Japan.
Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.
Srikrishnan, T. & Parthasarathy, R. (1987). *Int. J. Pept. Protein Res.* **30**, 557–563.

supplementary materials

Acta Cryst. (2013). E69, o660 [doi:10.1107/S1600536813008490]

L-Leucylglycylglycine

Masanori Ootaki, Yukino Nawa, Tomoko Hiroi, Hiroaki Matsui and Yoko Sugawara

Comment

A moderately large number of oligopeptides are biologically active, and their structures are investigated to facilitate the determination of the possible conformations of oligopeptide and polypeptide chains. The N-terminus and C-terminus of *L*-leucylglycylglycine (*L*-LGG) are protonated and ionized, respectively, and the molecule is a zwitterion (Fig. 1). The main chain is in a folded form. The torsion angles of C2—N2—C3—C4 and N2—C3—C4—N3 are -87.54 (18)° and -52.78 (19)°, respectively. The N-terminal $-\text{NH}_3^+$ groups and the C-terminal $-\text{COO}^-$ groups form hydrogen bond networks (Fig. 2 & Fig. 3). One of the hydrogen atoms of the $-\text{NH}_3$ group forms a three-centered hydrogen bond with the carboxyl and carboxyl oxygen atoms. In addition, intermolecular hydrogen bonds among amide groups ($\text{NH}\cdots\text{O}=\text{C}$) are formed along the *a* axis. The hydrophobic region composed of leucyl side chains is surrounded by hydrophilic parts, and forms a column along the *a* axis.

In the case of the *L*-leucylglycylglycylglycine (Srikrishnan & Parthasarathy, 1987), the main chain is a folded form, and hydrophobic columns are formed along the *a* axis as in the case of *L*-LGG. On the other hand, the main chain of *D,L*-leucylglycylglycine (*D,L*-LGG) (Goswami *et al.*, 1977) is in a nearly all-*trans* form except the N-terminus. The main chains align parallel to the *b* axis in a head-to-tail manner and a β -sheetlike structure is formed parallel to the *bc* plane. The hydrophobic regions of the leucyl side chains and the hydrophilic regions are aligned alternately along the *a* axis. As in the case of *D,L*-LGG, the main chain in *L*-leucylglycine 0.67 hydrate (Kiyotani & Sugawara, 2012) is in an extended form, and hydrophobic and hydrophilic regions are aligned alternately along the *c* axis.

Experimental

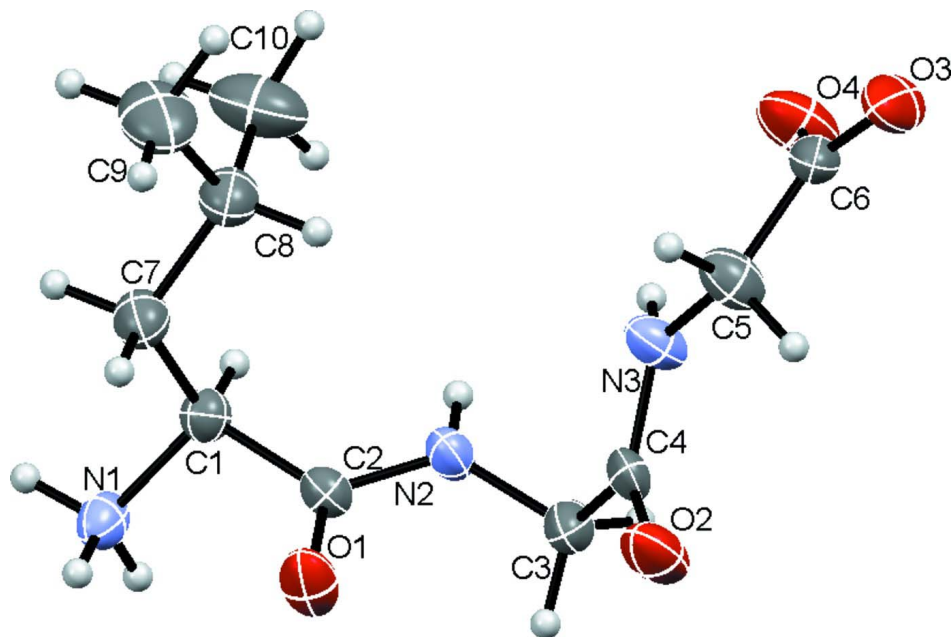
L-Leucylglycylglycine was purchased from Bachem Inc. Single crystals were obtained from an aqueous solution.

Refinement

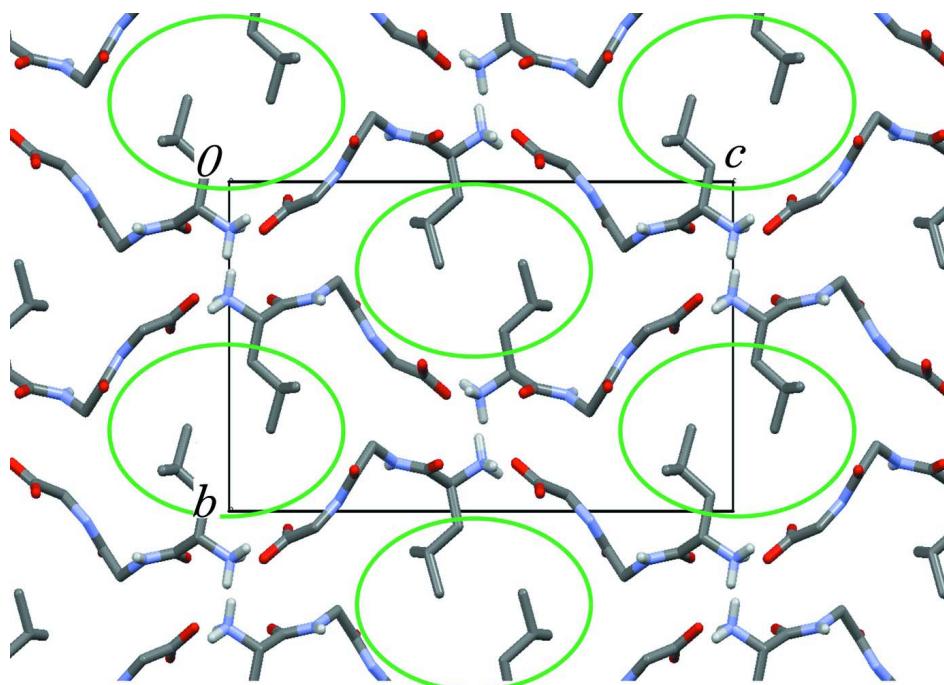
H atoms were placed in calculated positions with C—H = 0.98 Å (CH₃), 0.99 Å (CH₂) or 1.00 Å (CH) and refined in a riding mode with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$. The other H atoms were placed in a difference Fourier map. The N-terminal H atoms were restrained to N—H = 0.87 (4) Å during refinements. The absolute configuration was known for the purchased material.

Computing details

Data collection: *CrystalClear* (Rigaku, 2006); cell refinement: *CrystalClear* (Rigaku, 2006); data reduction: *CrystalClear* (Rigaku, 2006); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: Mercury (Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXL97* (Sheldrick, 2008) and *Yadokari-XG 2009* (Kabuto *et al.*, 2009).

**Figure 1**

View of the title compound with the atomic numbering scheme. Displacement ellipsoids are drawn at 50% probability level and H atoms are shown as small spheres of arbitrary radii.

**Figure 2**

Packing diagram of the title compound viewed along the *a* axis. Hydrophobic columns are indicated by green circles.

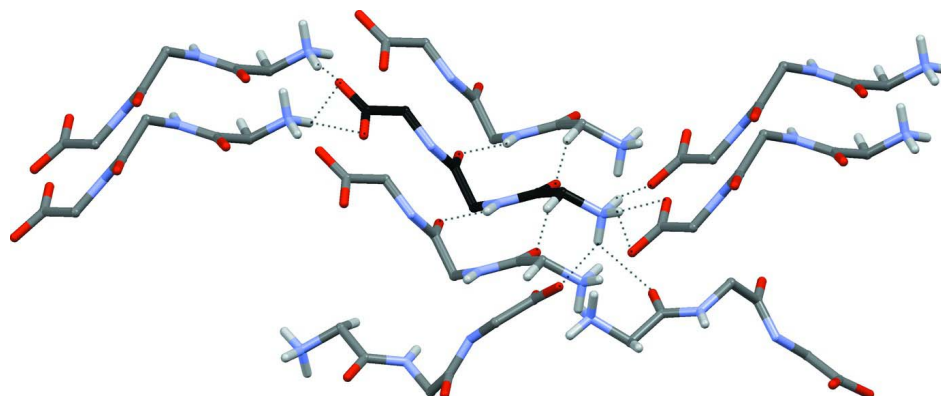


Figure 3

Hydrogen bonding scheme around the molecule, whose carbon atoms are colored with black. Hydrogen bonds are indicated by dotted lines. Side-chain atoms of the leucyl residues have been omitted for clarity.

***L*-Leucylglycylglycine**

Crystal data

$C_{10}H_{19}N_3O_4$

$M_r = 245.28$

Orthorhombic, $P2_12_12_1$

Hall symbol: P 2ac 2ab

$a = 5.391 (5) \text{ \AA}$

$b = 11.742 (10) \text{ \AA}$

$c = 19.975 (16) \text{ \AA}$

$V = 1264.4 (19) \text{ \AA}^3$

$Z = 4$

$F(000) = 528$

$D_x = 1.288 \text{ Mg m}^{-3}$

Mo $K\alpha$ radiation, $\lambda = 0.71070 \text{ \AA}$

Cell parameters from 949 reflections

$\theta = 7.6\text{--}17.5^\circ$

$\mu = 0.10 \text{ mm}^{-1}$

$T = 173 \text{ K}$

Block Rod, colorless

$0.48 \times 0.18 \times 0.08 \text{ mm}$

Data collection

Rigaku Mercury CCD area-detector
diffractometer

Radiation source: rotating anode

Graphite monochromator

ω scans

9374 measured reflections

2887 independent reflections

2200 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.070$

$\theta_{\text{max}} = 27.5^\circ$, $\theta_{\text{min}} = 3.5^\circ$

$h = -6 \rightarrow 6$

$k = -15 \rightarrow 15$

$l = -21 \rightarrow 25$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.038$

$wR(F^2) = 0.087$

$S = 0.96$

2887 reflections

176 parameters

3 restraints

Primary atom site location: structure-invariant
direct methods

Secondary atom site location: difference Fourier
map

Hydrogen site location: inferred from
neighbouring sites

H atoms treated by a mixture of independent
and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0374P)^2]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\text{max}} = 0.012$

$\Delta\rho_{\text{max}} = 0.14 \text{ e \AA}^{-3}$

$\Delta\rho_{\text{min}} = -0.17 \text{ e \AA}^{-3}$

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R -factors(gt) etc. and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
N1	−0.1744 (3)	0.64554 (12)	0.49670 (7)	0.0348 (3)
N2	−0.0484 (3)	0.64749 (12)	0.67001 (6)	0.0315 (3)
H5	−0.195 (4)	0.6402 (15)	0.6825 (9)	0.036 (5)*
N3	0.1814 (3)	0.52895 (12)	0.78349 (7)	0.0362 (3)
H8	0.022 (4)	0.5354 (16)	0.7880 (9)	0.048 (6)*
O1	0.2239 (2)	0.64148 (11)	0.58454 (5)	0.0415 (3)
O2	0.5246 (2)	0.62376 (11)	0.75146 (6)	0.0485 (3)
C1	−0.1911 (3)	0.58011 (12)	0.56075 (8)	0.0290 (3)
H4	−0.3570	0.5921	0.5820	0.035*
C2	0.0137 (3)	0.62595 (12)	0.60611 (7)	0.0273 (3)
C3	0.1320 (3)	0.69772 (14)	0.71523 (8)	0.0368 (4)
H6	0.0422	0.7431	0.7493	0.044*
H7	0.2381	0.7507	0.6894	0.044*
C4	0.2975 (3)	0.61277 (13)	0.75092 (7)	0.0314 (4)
C5	0.3059 (3)	0.45098 (16)	0.82883 (9)	0.0406 (4)
H9	0.4550	0.4883	0.8477	0.049*
H10	0.3604	0.3826	0.8038	0.049*
C6	0.1333 (4)	0.41541 (13)	0.88559 (8)	0.0354 (4)
O3	0.2277 (3)	0.35522 (11)	0.93090 (6)	0.0536 (4)
O4	−0.0855 (3)	0.44525 (12)	0.88306 (7)	0.0545 (4)
C7	−0.1526 (3)	0.45349 (13)	0.54488 (8)	0.0374 (4)
H11	−0.2711	0.4312	0.5094	0.045*
H12	0.0168	0.4434	0.5267	0.045*
C8	−0.1855 (4)	0.37232 (14)	0.60441 (9)	0.0413 (4)
H13	−0.0679	0.3959	0.6406	0.050*
C9	−0.1199 (5)	0.25116 (15)	0.58278 (10)	0.0636 (7)
H14	−0.1379	0.1995	0.6210	0.076*
H15	0.0518	0.2492	0.5667	0.076*
H16	−0.2316	0.2272	0.5467	0.095*
C10	−0.4475 (5)	0.3769 (2)	0.63228 (13)	0.0715 (7)
H17	−0.5664	0.3609	0.5964	0.086*
H18	−0.4796	0.4529	0.6507	0.086*
H19	−0.4656	0.3199	0.6678	0.086*
H1	−0.011 (5)	0.636 (2)	0.4768 (12)	0.089 (9)*
H2	−0.284 (5)	0.6147 (19)	0.4666 (12)	0.076 (7)*
H3	−0.202 (4)	0.7193 (16)	0.5047 (11)	0.058 (6)*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0420 (9)	0.0301 (7)	0.0322 (7)	−0.0012 (7)	−0.0133 (7)	0.0028 (6)
N2	0.0312 (8)	0.0404 (8)	0.0228 (6)	−0.0052 (7)	0.0020 (6)	0.0025 (6)
N3	0.0288 (8)	0.0458 (8)	0.0341 (7)	−0.0020 (7)	0.0000 (6)	0.0152 (6)
O1	0.0248 (6)	0.0666 (8)	0.0332 (6)	−0.0019 (6)	0.0030 (5)	0.0004 (6)
O2	0.0387 (8)	0.0668 (9)	0.0399 (7)	−0.0099 (7)	0.0061 (5)	0.0128 (6)
C1	0.0284 (8)	0.0304 (7)	0.0282 (8)	0.0006 (7)	−0.0021 (7)	0.0001 (6)
C2	0.0272 (8)	0.0294 (8)	0.0253 (7)	0.0018 (7)	0.0018 (6)	0.0038 (6)
C3	0.0496 (12)	0.0340 (8)	0.0268 (8)	−0.0083 (8)	−0.0054 (8)	0.0034 (7)
C4	0.0375 (10)	0.0396 (9)	0.0172 (7)	−0.0051 (8)	0.0031 (7)	0.0006 (6)
C5	0.0365 (10)	0.0480 (10)	0.0373 (9)	0.0046 (9)	0.0010 (8)	0.0148 (8)
C6	0.0498 (11)	0.0301 (8)	0.0264 (8)	−0.0120 (8)	−0.0017 (8)	0.0028 (7)
O3	0.0698 (9)	0.0532 (7)	0.0379 (7)	−0.0196 (7)	−0.0195 (7)	0.0220 (6)
O4	0.0427 (8)	0.0644 (9)	0.0562 (8)	0.0010 (7)	0.0156 (7)	0.0178 (7)
C7	0.0482 (11)	0.0303 (8)	0.0338 (9)	0.0007 (8)	−0.0012 (8)	−0.0004 (7)
C8	0.0532 (11)	0.0325 (8)	0.0381 (9)	−0.0025 (9)	−0.0036 (8)	0.0037 (8)
C9	0.096 (2)	0.0342 (10)	0.0602 (14)	0.0078 (10)	0.0029 (13)	0.0088 (9)
C10	0.0713 (16)	0.0552 (13)	0.0882 (17)	−0.0017 (12)	0.0223 (13)	0.0234 (12)

Geometric parameters (\AA , $^\circ$)

N1—C1	1.495 (2)	C5—C6	1.525 (3)
N1—H1	0.97 (2)	C5—H9	0.9900
N1—H2	0.92 (2)	C5—H10	0.9900
N1—H3	0.894 (19)	C6—O4	1.232 (3)
N2—C2	1.344 (2)	C6—O3	1.256 (2)
N2—C3	1.452 (2)	C7—C8	1.534 (2)
N2—H5	0.83 (2)	C7—H11	0.9900
N3—C4	1.336 (2)	C7—H12	0.9900
N3—C5	1.452 (2)	C8—C10	1.519 (3)
N3—H8	0.87 (2)	C8—C9	1.528 (3)
O1—C2	1.226 (2)	C8—H13	1.0000
O2—C4	1.231 (2)	C9—H14	0.9800
C1—C2	1.526 (2)	C9—H15	0.9800
C1—C7	1.534 (2)	C9—H16	0.9800
C1—H4	1.0000	C10—H17	0.9800
C3—C4	1.516 (2)	C10—H18	0.9800
C3—H6	0.9900	C10—H19	0.9800
C3—H7	0.9900		
C1—N1—H1	110.2 (15)	C6—C5—H9	109.5
C1—N1—H2	108.6 (14)	N3—C5—H10	109.5
H1—N1—H2	105 (2)	C6—C5—H10	109.5
C1—N1—H3	109.6 (14)	H9—C5—H10	108.1
H1—N1—H3	110 (2)	O4—C6—O3	125.31 (17)
H2—N1—H3	113 (2)	O4—C6—C5	118.43 (16)
C2—N2—C3	120.03 (15)	O3—C6—C5	116.25 (18)
C2—N2—H5	120.0 (13)	C8—C7—C1	115.23 (14)

C3—N2—H5	119.4 (13)	C8—C7—H11	108.5
C4—N3—C5	123.47 (17)	C1—C7—H11	108.5
C4—N3—H8	116.8 (13)	C8—C7—H12	108.5
C5—N3—H8	116.7 (13)	C1—C7—H12	108.5
N1—C1—C2	106.45 (13)	H11—C7—H12	107.5
N1—C1—C7	108.24 (13)	C10—C8—C9	110.59 (17)
C2—C1—C7	111.49 (13)	C10—C8—C7	111.68 (16)
N1—C1—H4	110.2	C9—C8—C7	109.41 (15)
C2—C1—H4	110.2	C10—C8—H13	108.4
C7—C1—H4	110.2	C9—C8—H13	108.4
O1—C2—N2	122.41 (14)	C7—C8—H13	108.4
O1—C2—C1	120.84 (14)	C8—C9—H14	109.5
N2—C2—C1	116.75 (14)	C8—C9—H15	109.5
N2—C3—C4	114.79 (14)	H14—C9—H15	109.5
N2—C3—H6	108.6	C8—C9—H16	109.5
C4—C3—H6	108.6	H14—C9—H16	109.5
N2—C3—H7	108.6	H15—C9—H16	109.5
C4—C3—H7	108.6	C8—C10—H17	109.5
H6—C3—H7	107.5	C8—C10—H18	109.5
O2—C4—N3	122.62 (16)	H17—C10—H18	109.5
O2—C4—C3	121.36 (15)	C8—C10—H19	109.5
N3—C4—C3	115.97 (17)	H17—C10—H19	109.5
N3—C5—C6	110.74 (16)	H18—C10—H19	109.5
N3—C5—H9	109.5		
C3—N2—C2—O1	4.0 (2)	N2—C3—C4—O2	129.75 (17)
C3—N2—C2—C1	−176.27 (13)	N2—C3—C4—N3	−52.78 (19)
N1—C1—C2—O1	−45.43 (19)	C4—N3—C5—C6	147.06 (16)
C7—C1—C2—O1	72.41 (19)	N3—C5—C6—O4	7.0 (2)
N1—C1—C2—N2	134.83 (14)	N3—C5—C6—O3	−174.41 (14)
C7—C1—C2—N2	−107.33 (16)	N1—C1—C7—C8	−175.12 (14)
C2—N2—C3—C4	−87.54 (18)	C2—C1—C7—C8	68.14 (19)
C5—N3—C4—O2	7.5 (2)	C1—C7—C8—C10	62.1 (2)
C5—N3—C4—C3	−169.93 (15)	C1—C7—C8—C9	−175.13 (17)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H \cdots <i>A</i>	<i>D</i> —H	H \cdots <i>A</i>	<i>D</i> \cdots <i>A</i>	<i>D</i> —H \cdots <i>A</i>
N1—H1 \cdots O3 ⁱ	0.97 (3)	1.78 (3)	2.743 (2)	168 (2)
N1—H2 \cdots O4 ⁱⁱ	0.92 (2)	1.94 (2)	2.822 (2)	160 (2)
N1—H2 \cdots O3 ⁱⁱ	0.92 (2)	2.52 (2)	3.260 (2)	138 (2)
N1—H3 \cdots O1 ⁱⁱⁱ	0.89 (2)	2.45 (2)	3.031 (2)	123 (2)
N1—H3 \cdots O3 ^{iv}	0.89 (2)	2.05 (2)	2.870 (2)	151 (2)
N2—H5 \cdots O2 ^v	0.83 (2)	2.05 (2)	2.832 (2)	155 (2)
C1—H4 \cdots O1 ^v	1.00	2.33	3.269 (2)	155

Symmetry codes: (i) $-x+1/2, -y+1, z-1/2$; (ii) $-x-1/2, -y+1, z-1/2$; (iii) $x-1/2, -y+3/2, -z+1$; (iv) $-x, y+1/2, -z+3/2$; (v) $x-1, y, z$.